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Multifocal ERG reveals long distance effects of a local bleach in the retina

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Abstract

To examine the distribution of ERG-activity in the central visual field after local bleaching of the fovea, multifocal electroretinograms were recorded in eight normal volunteers before, during and after recurrent light exposure. During bleaching (90% bleached pigment), the response density (scalar product) of the foveal area (0–2° eccentricity) decreased from 10.7 ± 3.5 to 4.1 ± 1.9 nV/degree^2 ($P < 0.001$). The average activity in the extrafoveal macular area was unchanged, while the amplitudes were frequently (in 53 of 54 areas) enhanced at 5–30.5° eccentricity. Here the average response density changed from 3.1 ± 0.9 to 3.5 ± 1.0 nV/degree^2 ($P < 0.001$). A fast recovery of foveal responses after cessation of bleaching occurred. Besides a strong decrease of response in the directly bleached area, local bleaching led to enhanced activity mainly 3–27° distant from the bleached area.

Keywords: Multifocal ERG; Electroretinography; Light adaptation; Bleaching; Cones

1. Introduction

Ganzfeld-electroretinography is an important technique in evaluating processes of light adaptation by an objective measurement of the retinal function. During the first 20 min of constant light adaptation the amplitudes of photopic flash and flicker ERG increase [1–3]. With increasing levels of light adaptation the photopic ERG amplitudes decrease due to a higher degree of bleached photoreceptor pigments [4]. In all these experiments, the background and stimulus intensity are nearly equally distributed over the retina. This is not true for the natural environment, however, where small sources of high light intensity often cause local light adaptation and bleaching of the photopigment, e.g. sunlight and electrical light sources. The effects of local light adaptation on the localization of the bleaching light have to be carefully discerned from the effects of this light on distant retinal neurons.

The multifocal ERG based on the m-sequence stimulation technique of Sutter [5–7] allows the simultaneous recording of numerous local electroretinograms from the posterior pole in a considerable short time. Bearse and Sutter [8] described a defect in regional activity caused by retinal lesions as well as by local bleaching. The present paper describes quantatively the spatial distribution of electroretinographic activity in the central 30° before, during, and after intense foveal light illumination.

2. Material and methods

2.1. Subjects

Eight normal volunteers (aged 21–33, median 26.5) were examined in this study. They had full visual acuity, refractive errors below ± 2.0 diopters and no history of eye disease or other relevant disorders. Informed consent was obtained from the subjects after a description of the procedures. The tenets of the declaration of Helsinki were followed and approval was ob-

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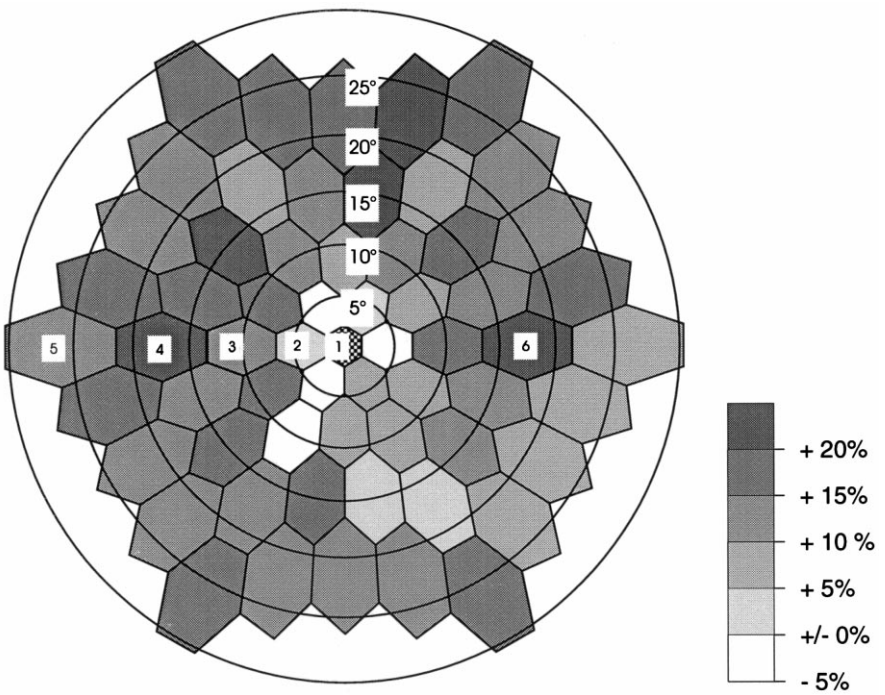

Fig. 1. Geometry of the test field with 61 hexagon within the central 30.5° visual field. Areas 1–5 along the horizontal meridian were chosen for detailed quantitative analysis. Area 6 indicates the area of the blind spot in the right eye. The change in response density in percent during light exposure is plotted in a grey-scale code. The bleach area is marked with a checkerboard pattern.

tained from the institutional Human Experimentation Committee.

2.2. Stimulation and recordings

The stimulus, consisting of 61 hexagons covering a visual field of 30°, was presented on a monitor with a frame rate of 75 Hz at a distance 28 cm from the subject's eye using the VERIS-scientific™ system (EDI, San Francisco, CA). The radius of the central hexagonal element was 2°. Since the element areas are scaled by eccentricity, the most eccentric areas are 4.7 times larger than the central area (Fig. 1). Each element, which was either black or white (93% contrast, mean luminance 48.5 cd/m^2), and changed independently from other elements following a binary m-sequence. A red central fixation point 2 mm in diameter was used.

Both eyes were dilated with tropicamide (0.5%) and phenylephrine (5%) to 7.5–8.5 mm and the refractive errors corrected. The ERG responses were recorded by means of DTL fiber electrodes (UniMed Electrode Supplies, UK) which were positioned on the conjunctiva directly beneath the cornea and attached with its two ends at the lateral and nasal canthus. The reference and ground skin electrodes (gold cup electrodes) were attached to the ipsilateral temple and forehead, respectively. The volunteers were adapted to ambient room light.

The signal was amplified ($\times$ 200000) and bandpass-filtered (10–100 Hz; Grass-amplifier, model 12, Quincy, USA). Each recording session was subdivided into 20 recording segments of approximately 11 s duration, during which the subjects were not allowed to talk or move. One recording of a multifocal ERG was performed before bleaching. We refer to this data as 'pre-exposure'.

2.3. Bleaching and recovery

During a recording time of about 4 min recovery from the bleaching from intense light can be expected. Therefore the principle approach was to reach a steady state of bleaching by recurrent light exposures between recording segments.

An indirect ophthalmoscope (Heine, Germany) held at the smallest available field stop at a distance of 15 cm from the subject's eye, served as a bleaching light source. The subjects fixated on the light source, that subtended an angle of 4.2° diameter. The retinal illuminance during bleaching was about 5×10^5 photopic Trolands in the fovea. This illumination bleaches more than 90% of the cone pigment [9]. The first period of bleaching was 15 s followed by a 15 s period in which a segment of the multifocal ERG was recorded. After each recording segment a period of 5 s bleaching was introduced. As in the pre-exposure recording the total number of segments was 20. The data of this experiment are referred to as 'during exposure'.

An additional multifocal ERG was recorded 20 s thereafter, i.e. within a period of 35–275 s after the

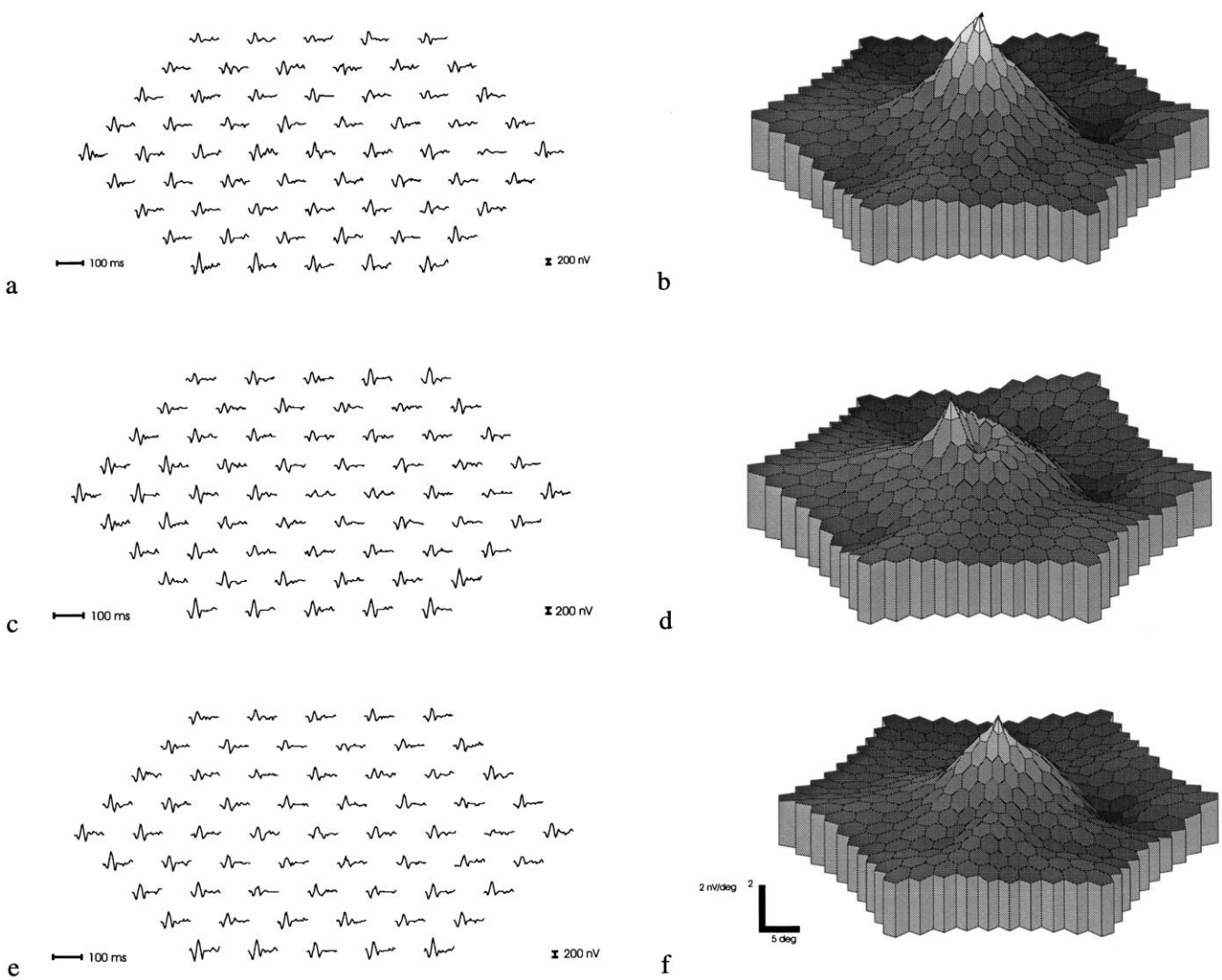

Fig. 2. Example of a recording pre-exposure (a) and (b); during exposure (c) and (d); and post-exposure (e) and (f). In the left panel the trace array of 61 local ERGs is plotted, and in the right panel the three-dimensional plot of the response density as a scalar product. In the recording of the right eye, a minimum is always evident from the blind spot (area 6 in Fig. 1). The main change during light exposure is the decrease of the foveal response, which recovers in the time after exposure.

previous bleaching, in order to document recovery ('post-exposure').

2.4. Data analysis

VERIS scientific software, using a fast m-transform algorithm [5,7] was employed for the calculation of the 61 local ERG responses from the measured signal. Specifically, first order kernels were used in this study because of their close correlation with the function of the outer retina [10]. From the resulting 61 ERG traces five local ERG from the horizontal meridian of the nasal field (temporal retina) were selected (Fig. 1)

Response densities were calculated as a scalar product, which is a dot product of the local response with a normalized template [6]. An average of all 61 elements served as a template. Additionally, peak-to-peak amplitudes and the implicit times of the first positive peak were measured. For statistical analysis a t-test was used.

3. Results

In each of the eight normal volunteers a multifocal electroretinogram with 61 local ERGs from the central 30.5° visual field was recorded with a minimum of activity occurring at the location of the blind spot. An example is presented in Fig. 2a, b. During bleaching of the fovea, the central response was depressed while all other responses remained without major changes (Fig. 2c, d). After cessation of bleaching, there was a recovery of the foveal response (Fig. 2e, f).

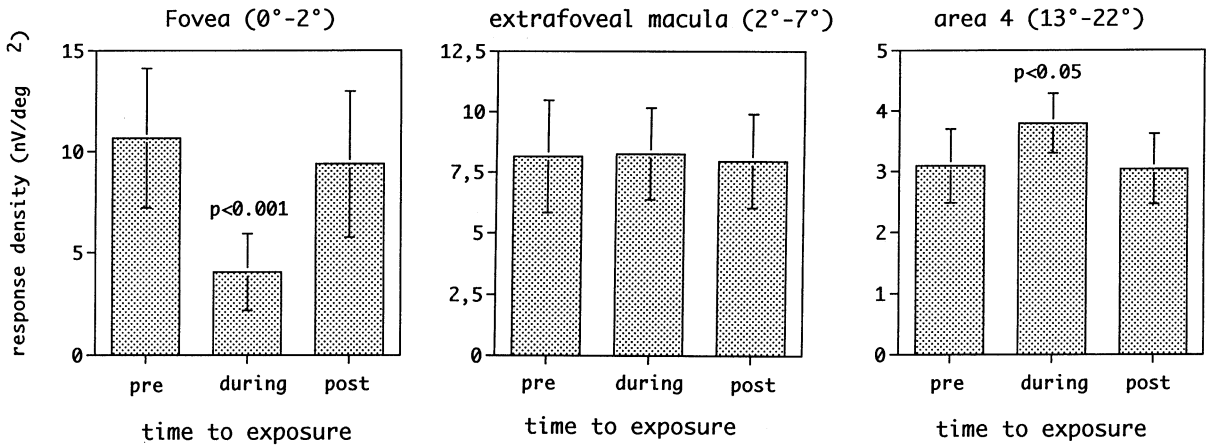

Fig. 3. Comparison of the mean response densities (± S.D.) as a scalar product for pre-, during, and post-exposure in three regions: (a) fovea (0–2°); (b) extrafoveal macula (2–7°); and (c) area 4 (13–22°).

The response density (scalar product) of the foveal region (area 1, 0–2° eccentricity) decreased from 10.7 ± 3.5 to 4.1 ± 1.9 nV/degree^2 during exposure ($P < 0.001$) and was 9.4 ± 3.6 nV/degree^2 post-exposure (Fig. 3a). In the extrafoveal macula (2–7° eccentricity) the response density remained unchanged with 6.7 ± 2.0 nV/degree^2 pre-exposure, 6.7 ± 1.6 nV/degree^2 during exposure, and 6.4 ± 1.7 nV/degree^2 post-exposure. In 53 out of 54 areas outside the macula (5–30.5° eccentricity) the response density was increased during bleaching. On average it changed significantly from 3.1 ± 0.9 to 3.5 ± 1.0 nV/degree^2 during bleaching. The post-exposure value was 3.0 ± 0.9 nV/degree^2. In Fig. 1 the amount of change in the response density during exposure is plotted for every single area. In Fig. 3b–c the changes are presented for areas 2 and 4 from Fig. 1. To document the changes during bleaching and recovery for each subject, ratios for the activity in the five selected areas were calculated (Fig. 4). In Fig. 4a the ratio between the response density during the exposure to the response density pre-exposure is plotted. For area 1 (fovea) the ratio is < 1.0 for each subject as expected, although the ratios show a remarkable variation. In the extrafoveal macular area (2–7°) four subjects presented a minor decrease in response (ratio < 1.0) and four a minor increase (ratio > 1.0), while in the areas from 7–30.5° the response density in all subjects was either stable or increased.

In Fig. 4b the ratio between post-expose response density to exposure response density is plotted. Ratios > 1.0 for the fovea demonstrate recovery of activity in this region.

The response density measurements using the peak-to-peak amplitudes revealed similar results. In the fovea the recovery was less pronounced than in the scalar product. The values were 70.2 ± 16.2 pre, 29.1 ± 7.3 during ($P < 0.001$), and 54.2 ± 13.0 nV/degree^2 post-exposure ($P < 0.05$ compared with the pre-exposure data). In area 4 (13–22° eccentricity) the response density increased significantly ($P < 0.05$) from 14.2 ± 2.1 to 19.2 ± 4.7 nV/degree^2 during exposure.

The foveal implicit time increased from 32.1 ± 2.1 pre to 34.2 ± 3.5 ms during exposure. There was a high variability of implicit time changes during the exposure: in one subject implicit time decreased by 5.0 ms and in an other it increased by 8.3 ms. The foveal post-exposure implicit time was 32.5 ± 1.5 ms. These changes were not statistically significant. Implicit times in other regions remained unchanged by light exposure and recovery.

In a control experiment we recorded two consecutive multifocal ERGs without any bleaching light in five volunteers. There were no major difference between the two measurements found. In area 4 the average values were 3.2 ± 0.5 and 3.17 ± 0.7 nV/degree^2.

4. Discussion

The depressing effect of strong foveal illumination was restricted to the foveal ERG. The average foveal response density during exposure to light, measured as a scalar product, was only 40% of the value measured before the exposure. The foveal ERG measured during the recovery time 35–275 s after the last bleaching light exposure had 90% of the pre-exposure value.

The strong bleaching light left the function of retinal structures in the immediate vicinity of the exposed area unaltered. On average, at 5–30.5° eccentricity there was a moderate but significant increase of amplitude to 112.9% of the pre-exposure values.

Weiner and Sandberg [11] found that the foveal ERG amplitude increased during consecutive examinations. In a control experiment we did not find such an increase of local responses under the light conditions used in our multifocal ERG protocol. The multifocal ERG

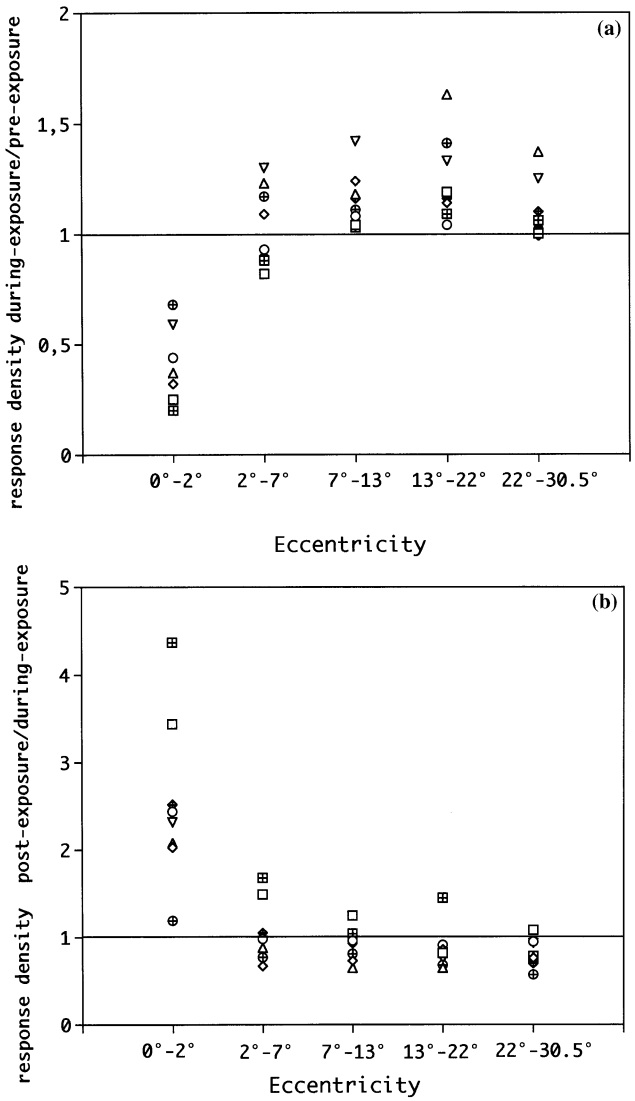

Fig. 4. (a) The ratio of the response density during exposure to the response density pre-exposure at different eccentricities. Each symbol represents an individual subject. (b) The ratio of the response density post-exposure to the response density during exposure at different eccentricities. Each symbol represents the same subject as in (a).

in area 4 (13–22°) that was marked by an amplitude increase of 25%, remained unchanged in the average results of 5 volunteers during re-testing without bleaching.

The light adaptation level in the extrafoveal regions should be higher during exposure compared to pre-exposure due to stray light and light reflected from the fovea. A higher level of light adaptation should lead to a decrease of amplitude and a shorter implicit time [4]. Paradoxically, the amplitudes recorded from areas distant from the exposed area are increased, and the implicit times remained unaltered. A possible explanation for this result is a change in neuronal adaptation by lateral connections induced by focal central illumination. Especially the horizontal cells have electrophysiological influence far beyond their anatomical extension [12]. Changing the connectivity of this network by local illumination may result in functional alterations of distant retinal areas.

Multifocal ERG allows a detailed description of the topography of electrophysiological effects of a local bleaching light. The principle finding of this study was the enhancement of the activity in regions distant from the exposed area.

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